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Lack of reproduction of the hallmark porcine circovirus type 2-associated lesions in a mouse model

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Summary and Implications

BALB/c, C57BL/6, and C3H/HeN mice were experimentally-infected with porcine circovirus type 2 (PCV2). The mice were tested for their ability to become infected with porcine circovirus type 2 (PCV2) and to develop the hallmark PCV2-associated lymphoid depletion and histiocytic replacement of lymphoid follicles characteristic of postweaning multisystemic wasting syndrome. Since immunostimulation has been shown to increase PCV2-replication in the pig, half of the mice were immunostimulated with keyhole limpet hemocyanin in incomplete Freund's adjuvant (KLH/ICFA) at the time of PCV2-inoculation. PCV2 inoculation was done twice at 4 and 5 weeks of age by using intramuscular and intranasal routes. Necropsies were performed in 5-day-intervals at 12, 17, 22, 27, 32, and 37 days post PCV2 inoculation. None of the mice developed clinical disease and none of the mice developed PCV2-associated lymphoid lesions. Immunohistochemistry (IHC) and in-situ-hybridization (ISH) for PCV2-antigen/nucleic acids was performed on all tissues of all mice and was negative. PCR was done on pooled tissues and serum samples obtained at necropsy. The majority of the mice (101/111 PCV2 infected mice) were positive for PCV2-nucleic acids in tissue samples. Forty-one percent of the mice (46/111 PCV2 infected mice) were positive for PCV2-nucleic acids in serum samples. There was no difference between treatment groups or lines. This study confirms that mice can be infected with PCV2 and could be important in the epidemiology of PCV2; however, the mouse model may not be useful to understand the pathogenesis of PCV2-associated lesions.

Introduction

The unique and hallmark lesions of PCV2 associated PMWS is lymphoid depletion and histiocytic replacement of follicles in the lymphoid tissues. We have a well characterized pig model for PCV2-infection. PCV2 is ubiquitous in the swine population and we have yet to locate herds free of PCV2-specific antibodies. This makes it very difficult to get PCV2 virus and antibody free pigs for research. We also suspect that there are differences in host susceptibility to PCV2-associated diseases and a genetically well characterized host such as the mouse is needed to further investigate differences in host susceptibility to PCV2.

Materials and Methods

Animals: Three different mouse lines (BALB/c, C57BL/6 and C3H/HeN) consisting of 48-50 mice for each line were used in this study. The mice were purchased at 3 weeks of age and randomly assigned to treatment groups.

Experimental design: Half of the mice received KLH/ICFA at 4 and 6 weeks of age. Each mouse received 0.05 ml subcutaneously in the tail base and posterior cervical area. Twelve mice in each line served as negative control mice. The remaining mice in each line were inoculated with PCV2 isolate 40895 at 4 and 5 weeks of age intramuscularly and intranasally.

Necropsy: At necropsy, samples of lymph nodes, liver, spleen, lung, intestine, thymus, kidney, and heart were collected in 10% neutral-buffered formalin for microscopic evaluation and frozen for PCR.

Histopathology and demonstration of PCV2: Tissue sections of all mice were evaluated for the presence of microscopic lesions and for the presence of PCV2-antigen by IHC and for the presence of PCV2-nucleic acids by ISH.

Serology: ELISA for the detection of PCV2-specific antibodies and PCR for the detection of PCV2-nucleic acids were done on the serum samples of all mice collected at necropsy.

Results and Discussion

None of the mice was clinically affected and no weight loss or respiratory disease typical of PMWS was observed. Macroscopic lesions were limited to enlarged lymph nodes which appeared to be most prominent in the BALB/c mice. The majority of the mice (91%; 101/111 PCV2-infected mice) within all lines and treatment groups was PCR positive on tissue pools. PCR on serum revealed 59.5% (22/37) positive BALB/c mice, 25.0% (9/36) positive C57BL/6 mice, and 39.5% (15/38) positive C3H/HeN mice. There was no difference between mice that received KLH/ICFA and those that did not. There was no evidence for PCV2-associated microscopic lesions in any of the mice: none of the mice developed lymphoid depletion and granulomatous lymphadenitis as seen in pigs. PCV2 was not detected in any of the mice tissues by IHC or ISH. Based on ELISA, none of the mice seroconverted to PCV2 during the duration of the study.

The results of this study indicate that mice may not be a useful model to understand the pathogenesis of PCV2-associated lesions. However, mice may be able to replicate PCV2 and transmit it within and between farms.

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